

### **REMARKS**

Claims 1-4 and 6 are all the pending claims. Claims 5, 7 and 8 are canceled, and claims 1-4 and 6 are rejected.

#### **I. Information Disclosure Statement (IDS)**

On page 2 of the Office Action, the Examiner states that the previously cited foreign patent documents and non-patent literature publications have not been considered because copies of such documents are required under 37 CFR 1.98(a)(2).

Applicants hereby submit a supplemental IDS along with copies of the cited foreign patent documents and non-patent literature publications.

#### **II. Response to Claim Rejections Under 35 U.S.C. § 103**

Claims 1-4 and 6 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Furcht *et al.* (U.S. Patent No. 7,015,037, “Furcht”), in view of Kokuzawa *et al.* (U.S. Patent Application Publication No. 2006/0134078, “Kokuzawa”).

In making the rejection, the Examiner relies upon Furcht to teach culturing mesenchymal stem cells or multipotent adult stem cells (MASCs) to differentiate the cells into different cells including neural cells. Furcht is also relied upon to disclose that the MASCs are confluent cultured prior to differentiation. In particular, the Examiner states “Differentiation to any muscle phenotype required that MASCs be allowed to become confluent prior to induction of differentiation.” *Office Action of April 29, 2008*, first full paragraph on page 3.

Applicants respectfully disagree.

First, Furcht fails to teach confluent MASCs culture prior to the neural differentiation as defined in the present claim 1.

It is noted that Furcht teaches differentiation of MASCs into neural cells. *See* Example 5. However, Furcht fails to teach confluent MASCs as a pretreatment prior to the neural differentiation. The portion of Furcht reference, to which the Examiner relies to allege that Furcht teaches confluent culture of MASCs prior to differentiation into neural cells, teaches differentiation of mesenchymal stem cells into bone or muscle cells, not differentiation into neural cells. Indeed, Furcht discloses that MASCs are culture to be confluent prior to differentiating into bone or muscle cells, while expressly avoiding confluence of MASCs prior to differentiating into neural cells.

Kokuzawa fails to cure the defects of Furcht because Kokuzawa does not even disclose any MASC.

To establish *prima facie* obviousness of a claimed invention, all the cited references must recite all the claim limitations. *In re Royka*, 490 F.2d 981, 984 (CCPA 1974). For the reasons previously presented above, Applicants contend that neither Furcht, Kokuzawa, nor the other cited references, alone or in combination, teach or suggest all the claim limitations of the invention, either explicitly or inherently. In particular, these references, alone or in combination, do not expressly or inherently teach the “confluent culturing [of] the mesenchymal stem cell as a pretreatment” as recited in claim 1. Thus, these references do not support a *prima facie* case of obviousness.

Not only Furcht fails to teach the confluent mesenchymal stem cells prior to neural differentiation, Furcht *teaches away* from the presently claimed confluent culture of mesenchymal stem cells, as a pretreatment, for neural differentiation. Specifically, with regard to the MASC culture for neural differentiation, Furcht's specification states, "[c]ulture at high density ... was also associated with loss of expansion capacity, and cells did not proliferate beyond 25-30 cell doublings" (column 46, lines 9-12), and "[c]ell densities were maintained between  $2-8 \times 10^3$  cells/cm<sup>2</sup>," instead of reaching the confluency (column 45, lines 41-42; & column 49, lines 41-42).

As discussed above, Furcht clearly avoids confluence of MASCs prior to differentiating them into neural cells, while teaching confluent culture of MASCs prior to differentiating them into bone or muscle cells. One skilled in the art, from the reading of Furcht, would not have been motivated to confluent culture MASCs prior to differentiating them into neural cells. The Examiner fails to establish a reason as to why one of ordinary skill would pursue the technique for differentiating into muscle cells in differentiating into neural cells. Rather than indicating why one of skill in the art would choose to combine such elements, the Examiner is silent. As the Supreme Court recently discussed, the "apparent reason to combine the known elements in a fashion claimed by the [claims] at issue ... should be made explicit." *KSR International Co. v. Teleflex Inc.*, 550 U.S. -, 82 USPQ2d 1385, 1395 (2007).

It is noted that Kokuzawa teaches a culture medium to differentiate neural stem cell into a neural cell. However, it fails to teach a culture medium to differentiate MASCs into a neural cell.

There must be a reasonable expectation of success in combining cited references. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) and MPEP 2143.02. One of

ordinary skill in the art would have no reasonable expectation of success in incorporating the medium for the differentiation of Kokuzawa's neural stem cells isolated from striatal cells in the differentiation of MASCs because it is well-known in the art that the properties of mesenchymal cells are different from those of neural stem cells.

Finally, Applicants respectfully submit that the confluent pretreatment of MASCs prior to differentiating into a neural cell shows much improved differentiation and proliferation of neural cell, compared to differentiating MASCs into a neural cell in a same medium, without prior confluent culture. *See* Table 3 on page 23 of the specification. Additionally, such improved culture efficiency resulted from the confluent culture prior to the differentiating is expected to reduce the risk of contamination and the overall cost and time consumed in the differentiation process.

### CONCLUSION

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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